PKLR gene

pyruvate kinase, liver and RBC

Normal Function

The *PKLR* gene is active (expressed) in the liver and in red blood cells, where it provides instructions for producing an enzyme called pyruvate kinase. This enzyme is involved in a critical energy-producing process known as glycolysis. During glycolysis, the simple sugar glucose is broken down to produce energy. Specifically, pyruvate kinase is involved in the last step of the glycolytic pathway. In this step, a cluster of oxygen and phosphorus atoms (a phosphate group) is moved from a molecule called phosphoenolpyruvate to another molecule called adenosine diphosphate (ADP), resulting in molecules called pyruvate and adenosine triphosphate (ATP). ATP is the cell's main energy source.

Health Conditions Related to Genetic Changes

pyruvate kinase deficiency

More than 200 mutations in the *PKLR* gene have been identified in people with pyruvate kinase deficiency. People with this disorder have two *PKLR* gene mutations in each cell. Most of the mutations that cause pyruvate kinase deficiency replace single protein building blocks (amino acids) in the pyruvate kinase enzyme or result in an enzyme that is abnormally short. The mutations lead to reduced pyruvate kinase enzyme function, causing a shortage of ATP in red blood cells and increased levels of other molecules produced earlier in the glycolysis process. The abnormal red blood cells are gathered up by the spleen and destroyed.

The resulting shortage of oxygen-carrying red blood cells (anemia) leads to extreme tiredness (fatigue), unusually pale skin (pallor), and shortness of breath. Iron and a molecule called bilirubin are released when red blood cells are destroyed, resulting in an excess of these substances circulating in the blood. Excess bilirubin in the blood causes yellowing of the eyes and skin (jaundice) and increases the risk of developing small pebble-like deposits in the gallbladder or bile ducts (gallstones).

other disorders

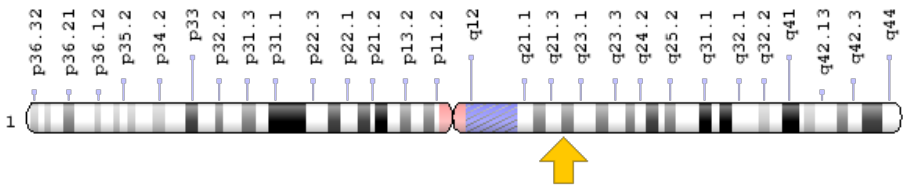
Researchers believe that people who have one copy of a *PKLR* gene mutation in each cell may be partially protected against malaria, an infectious disease carried by a certain type of mosquito. Mutations that lead to a reduction in the amount of functional pyruvate kinase appear to make it more difficult for this parasite to invade red blood cells. Studies indicate that individuals from populations in Africa, where

malaria is a frequent cause of death in children, carry one copy of a mutated *PKLR* gene in each cell more than twice as often as individuals of European descent. The increased frequency of *PKLR* gene mutations may contribute to resistance against malaria in these African populations.

Chromosomal Location

Cytogenetic Location: 1q22, which is the long (q) arm of chromosome 1 at position 22

Molecular Location: base pairs 155,289,293 to 155,301,434 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- KPYR_HUMAN
- PK1
- PKL
- PKR
- PKRL
- pyruvate kinase 1
- pyruvate kinase isozyme R/L
- pyruvate kinase type L
- pyruvate kinase, liver and blood cell
- R-type/L-type pyruvate kinase
- red cell/liver pyruvate kinase
- RPK

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): The Glycolytic Pathway is Tightly Controlled
  https://www.ncbi.nlm.nih.gov/books/NBK22469/#A2292

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PKLR%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- PYRUVATE KINASE, LIVER AND RED BLOOD CELL
  http://omim.org/entry/609712

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PKLR.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PKLR%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=9020
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5313
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